REMARKS

The April 14, 2006 Official Action has been carefully considered. In view of the amendments submitted herewith and these remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset, it is noted that a shortened statutory response period of 3 months was set in the April 14, 2006 Official Action. Accordingly, the initial response period is due to expire July 14, 2006. The present amendment and request for reconsideration is being filed before the expiration of the initial response period.

It is also noted preliminarily that claim 29 has been examined only to the extent of the elected protein, i.e., LOMT 21. For the reasons already made of record during the telephone interview which took place on June 28, 2005 and in the traverse of the restriction requirement, applicants still contend that the maintenance of the requirement for restriction is unwarranted and onerous. Indeed, if claim 29 were limited as required by the Examiner, a competitor would be free to use a non-elected protein which has been identified by the inventors in a screening method and not literally infringe the claim. However, in order to expedite allowance of the instant application, claim 29 is hereby cancelled without prejudice to applicants' right to file one or more continuing applications on the subject matter encompassed by this claim and the other claims which have been withdrawn. Identification of differential expression of any of the proteins recited in claim 29 is protected in any case, as such a step is encompassed by the generic language of claim 1.

Turning to the substantive aspects of the April 14, 2006 Official Action, claims 1-3, 5-7, 14-25, 27-33, 52 and 53 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Specifically, the Examiner asserts that the claim language "comparatively insulin-sensitive subject", which

appears in claims 1, 5, 16 and 53, is unclear in the absence of a specified basis for comparison.

Claims 1-3, 5, 14, 15, 18-20, 27, 28, 52, and 53 have also been rejected under 35 U.S.C. §102(b) as allegedly anticipated by Wang et al. (Br. J. Pharm., 122:1405-10 (1997)).

Claims 1-3, 5, 14, 15, 18-20, 27, 28, 52 and 53 have been further rejected under 35 U.S.C. §103(a) as allegedly obvious in view of the combined disclosures of Wang et al., supra, and U.S. Patent 5,744,300 to Linskens et al. Linskens et al. is cited for its disclosure of high-throughput screening for identification of compounds that alter differential gene expression levels in relation to senescence-related genes.

Considering Wang et al. In combination with Linskens et al., the Examiner contends that it would have been obvious to a person of ordinary skill in the art at the time the present invention was made to employ high-throughput methodology of identifying differentially expressed genes as purportedly disclosed by Linskens et al., for isolating and characterizing the differentially expressed proteins (DEPs)identified by Wang et al., because the isolation, characterization and high-throughput screening techniques purportedly disclosed by Linskens et al. are generally applicable to systems comprising differentially expressed genes.

The foregoing rejections constitute all of the grounds set forth in the April 14, 2006 Official Action for refusing the present application.

In accordance with the present amendment, claim 1 has been amended to include a recitation of "untreated insulin resistance subject", and to change "comparatively insulin-sensitive subject" to "insulin-sensitive in comparison to said untreated insulin resistant subject". Support for the former change is provided in the present specification at page 24, lines 4 and 5, whereas the latter change finds support at page 21, lines 26-31. Claim 1 has been further amended to call for the steps of "determining the effect of said agent on the level of expression of said at least one differentially expressed protein in said fifth biological sample; and identifying an

agent which alters the expression level towards that observed in the second or third biological sample as an agent having efficacy for the treatment of insulin resistance". Support for this addition to claim 1 is provided in the present specification at page 44, lines 11-20, which is part of the description under the heading "Screening for agents to ameliorate insulin resistance" (see page 42). This amendment also cancels claim 29 and the claims that had been withdrawn from consideration (claims 34-51), in order to advance the prosecution of this application to allowance.

Entry of the present amendment is respectfully requested, inasmuch as this amendment neither introduces new matters nor requires further examination or search, and it clearly place the application in condition for allowance. In any event, entry of the present amendment would materially reduce the issues that would need to be addressed on appeal, should an appeal be necessary in this case. This amendment was not presented earlier, because the rejections and/or arguments to which it responds were raised for the first time in the April 14, 2006 Official Action.

As a result of the foregoing amendment, any indefiniteness that may have been engendered by the recitation of "comparatively insulin-sensitive subject" in claims 1, 5, 16 and 53 has now been eliminated. Accordingly, the only matters remaining to be addressed are the anticipation and obviousness rejections of claims 1-3, 5, 14, 15, 18-20, 27, 28, 52 and 53 based on Wang et al., and the combination of Wang et al. and Linskens et al., respectively. For the reasons given hereinbelow, these grounds of rejection are respectively traversed.

A. The Disclosure of Wang et al. Fails to Anticipate Claims 1-3, 5, 14, 15, 18-20, 27, 28, 52 and 53

A rejection under 35 U.S.C. §102 is proper only when the claimed subject matter is identically disclosed or described in the reference cited as evidence of anticipation. In re Arkley, 172 USPO 524 (CAPA 1972). To the same effect is Ex parte

Drewe, 203 USPO 1127 (PTO Bd. Apps. 1978) (all claim recitations must be satisfied for a prior art reference to be a complete anticipation of the claimed invention). Applying these well-established principles to the present case, the 35 U.S.C. §102(b) rejection of claims 1-3, 5, 14, 15, 18-20, 27, 28, 52 and 53 based on Wang et al. is improper because the subject matter of those claims is nowhere identically disclosed or described in the cited reference.

Claim 1, as now amended, calls for a 5-step method of screening for an agent having efficacy in treating insulin resistance. In the first step, four separate biological samples are obtained from subjects who are: insulin resistant and untreated; insulin resistant and treated with a known treatment or compound that alters insulin sensitivity; normal or insulin-sensitive in comparison to untreated insulin resistant subject; normal and treated with a known treatment or compound that alters insulin sensitivity or insulin-sensitive in comparison to the untreated insulin resistant subject and treated with a known treatment or compound that alters insulin sensitivity. In the second step, at least one protein differentially expressed between the biological samples obtained in step 1 is identified. The third step involves providing a fifth biological sample which comprises cellular tissue susceptible to insulin action or a sub-cellular fraction thereof obtained from an insulin resistant subject and which has been treated with the agent that is being screened for insulin resistance treatment efficacy. The effect of the agent undergoing screening on the expression level of at least one DEP is determined in the fourth step. In the fifth step, an agent which alters the expression level towards that observed in the second or third biological sample is identified as having efficacy for the treatment of insulin resistance.

Wang et al. does not describe a screening method for identifying agents having efficacy in treating insulin resistance. Nor does Wang et al. suggest that a DEP expression pattern, such as recited in applicants' claim 1, would have any practical utility, much less as a screen for such agents.

Rather, the study reported in Wang et al. is simply an assessment of the effects of known treatments.

Assuming for the sake of argument that the first two steps of the claimed method are disclosed by Wang et al., the same cannot be said for the third, fourth and fifth steps of the method. Simply put, Wang et al. does not disclose a method in which a fifth biological sample is provided, or in which a determination is made of the effect produced by the agent undergoing screening on the level of expression of at least one DEP in the fifth biological sample, or in which an agent which alters the expression level towards that observed in the second or third biological sample is identified as having efficacy for the treatment of insulin resistance.

Inasmuch as Wang et al. plainly fails to identically disclose or describe all of the claim recitations of applicants' claims 1-3, 5, 14, 15, 18-20, 27, 28, 52 and 53, the 35 U.S.C. §102(b) rejection of those claims based on Wang et al. is improper and should be withdrawn.

Furthermore, applicants take exception, with all due respect, to the Examiner's contention that claim 1 does not exclude embodiments in which the agent undergoing screening may also be the known compound that alters insulin sensitivity, i.e., in step (a)(iii) of the claimed method.

It is axiomatic that, in proceedings before the PTO, claims in an application are to be given their broadest reasonable interpretation consistent with the specification, and that claim language should be read in light of the specification as it would be interpreted by one of ordinary skill in the art. In re Bond, 15 USPQ 2d (1566 Fed. Cir. 1990). The Examiner apparently is unfamiliar with this axiom. Otherwise, he would not have accorded claim 1 the preposterous interpretation set out at page 6 and again at page 11 of the April 14, 2006 Official Action.

The objective of claim 1 is plainly spelled in its preamble, i.e., "a method of screening for an agent having efficacy in treating insulin resistance". Moreover, steps (d) and (e) of claim 1 specifically call for determining the effect

of the agent on the level of expression of at least one DEP in the fifth biological sample, and identifying an agent which alters the expression levels towards that observed in the second or third biological sample as an agent having efficacy for the treatment of insulin resistance. It is self-evident that these are screening steps.

That the present invention is concerned with screening for agents having utility in treating insulin resistance is also made abundantly clear from the Abstract and the specification of this application. See, for example, page 7, lines 6-25, page 13, line 24 through page 16, line 21 and page 42, line 33 through page 46, line 8.

"Screening" is a term of art in the field of drug discovery, and is understood by those skilled in the art to refer to testing of compound "libraries" for their ability to modify a chosen target for a particular disease. This is precisely the context in which the term "screening" is used in applicants' specification and claims. Applicant is unaware of any factual basis, and the Examiner has cited none, that would tend to support the Examiner's interpretation that the screening method of claim 1 encompasses the screening of the known compounds, such as BRL 49653, which are used in step 1) of the method for the treatment of subjects to alter insulin sensitivity, as is repeatedly asserted in the April 14, 2006 Official Action.

In light of the claim interpretation axiom quoted in In re Bond, supra, it must be concluded that the Examiner has adopted a construction of claim 1 beyond that which is reasonably based on the description of screening methodology in applicants' specification and the art-recognized meaning of the term "screening". Cf., In re Baker Hughes, Inc., 55 USPQ 2d 1149 (Fed. Cir. 2000) (court reversed prior art rejection based on PTO Board of Appeals' error in construing claim term "hydrocarbon" to include gases, which court found unreasonable in light of the totality of the written description).

For this reason also, the 35 USC §102(b) rejection of claims 1-3, 5, 14, 15, 18-20, 27, 28, 52 and 53 based on Wang et al. is untenable and should be withdrawn.

B. The Combined Disclosures of Wang et al. and Linskens et al. Fail to Render Obvious Claims 1-3, 5, 14, 15, 18-20, 27, 28, 52 and 53

Concerning the rejection of claims 1-3, 5, 14, 15, 18-20, 27, 28, 52 and 53 based on Wang et al. in view of Linskens et al., the Examiner's position in this regard is untenable for at least the same reasons discussed above with respect to the impropriety of the §102(b) rejection of the same claims based on Wang et al. Since Linskens et al. does not compensate for the fundamental deficiencies noted above in the disclosure of Wang et al., the rejection of claims 1-3, 5, 14, 15, 18-20, 27, 28, 52 and 53 based on the combined disclosures of these two references is improper and should also be withdrawn.

An objective reading of Wang et al. and Linskens et al. reveals nothing that would motivate one skilled in the art to combine their disclosures in the manner proposed by the Examiner. Indeed, the disclosures of Wang et al. and Linskens et al. are entirely unrelated. Wang et al. discloses an examination in fatty (insulin resistant) Zucker rats and lean (insulin-sensitive) Zucker rats when treated and not treated with a known treatment, namely, BRL 49653. By contrast, Linskens et al. describes the identification of differentially expressed mRNA. The reason why these are not equivalent tools for identifying the molecular basis of a disease process, such as insulin resistance disorders, is explained at page 5, lines 11-16 of the present application. Briefly, changes in protein expression can be much more complex than changes in mRNA expression, since the amount of protein present is influenced by the turnover rate of the corresponding mRNA, the turnover rate of the proteins themselves, interactions with other proteins and post-translational modifications such as phosphorylation. It is changes in protein expression (rather than RNA expression) which underlie the development of

disorders such as insulin resistance disorders. Therefore, monitoring the level of the protein itself gives a much more accurate picture of the disease state than does monitoring mRNA levels, and so is much more useful for studying the effects of candidate therapeutic agents.

In view of the clear distinctions between the applicants' claimed screening method and the cited references, as discussed above, is quite apparent that the Examiner has used Applicants' disclosure as a guide for combining unrelated prior art teachings in an effort to make out a case of *prima facie* obviousness. Such hindsight reconstructions has long been held impermissible, since it is contrary to the standard of obviousness set forth in 35 U.S.C. §103, which requires a determination of whether the claimed subject matter as a whole would have been obvious at the time the invention was made, based on the state of the art as reflected in the cited references, and without benefit of Applicants' disclosure. Neither of the references relied on by the Examiner in support of the §103(a) rejection of claims 1-3, 5, 14, 15, 18-20, 27, 28, 52 and 53 contains the slightest suggestion to use what is disclosed in one reference in combination with what is disclosed in the other reference. Cf. In re Avery, 186 USPQ 161 (CCPA 1975). That being the case, it cannot reasonably be maintained that the combined disclosures of Wang et al. and Linskens et al. fairly suggest doing what the Applicants have done. It must be concluded, therefore, that this rejection is based on impermissible hindsight. Cf. Ex parte Stauber, 208 U.S.P.Q. 945 (Bd. Apps. 1980).

For all the foregoing reasons, the prior art references cited in support of the §103(a) rejection in this case, consdiered singly or together, neither teach nor suggest the claimed subject matter as a whole, and as such, fail to establish that Applicants' invention is *prima facie* obviousness. Accordingly, the rejection of claims 1-3, 5, 14, 15, 18-20, 27, 28, 52 and 53 under 35 U.S.C. §103(a) based on the combined disclosures of Wang et al. and Linskens et al. is improper and should be withdrawn.

In view of the present amendment and the foregoing remarks, it is respectfully urged that the rejections set forth in the April 14, 2006 Official Action be withdrawn and that this application be passed to issue, and such action is earnestly solicited.

The present communication is completely responsive to the issues raised in the Official Action of April 14, 2006. Applicants believe that the claims as they stand are in condition for allowance. In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number given below.

Respectfully submitted,

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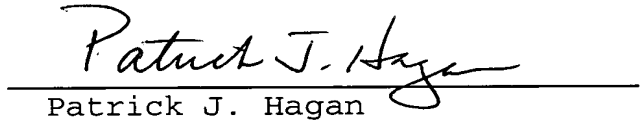
By 

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